4. (Second Amendment) A DNA according to claim 2 encoding a protein wherein the hinge region is from an immunoglobulin-like protein.

REMARKS

Claims 1-15 are pending in this application. Claims 1, 8, 12 and 14 are withdrawn on account of a restriction requirement. Claims 2, 3 and 4 are herewith amended. No claims are added or deleted. Thus, claims 1-15 are pending and claims 2-7, 9-11, 13 and 15 are active in this case. A marked-up copy of the claims, as amended is attached.

I. Rejections under 35 USC § 112

The Examiner has rejected claims 1, 3 and 4 under 35 USC § 112, second paragraph. Specifically, the Examiner states that claim 1 is dependent upon a non-elected claim. Claim 3 is said to be unclear as to whether it is limited to FRP5 and as to whether the FRP5 antibody refers to the antigen binding domain of part 1 of claim 2. Claim 4 is said to be unclear as to how an "immunoglobulin-like" hinge region differs from an immunoglobulin hinge region.

In response, applicants note that claim 1 is withdrawn from consideration on account of the restriction requirement. Clarification of the Examiner's intent is respectfully requested. With regard to claim 3, applicants traverse this rejection but further urge that this rejection is rendered moot with the above amendment. With regard to claim 4, applicants clarify that it is not the "hinge" which is intended to be "immunoglobulin-like". Rather, applicants intend to claim a hinge from a protein that is "immunoglobulin-like". Support for the clarifying amendment can be found in the specification at page 9, last paragraph, to page 10, first paragraph.

The Examiner further rejects claim 3 for lack of a written description and for lack of enablement. Specifically, the Examiner states that there is not complete evidence that the claimed biological materials are known and readily available to the public. The Examiner explains the procedure for reliance upon a biological deposit.

In response, applicants explain that the FRP5 is fully described in the prior art. For instance, U.S. Patent No. 5,571,894 provides a detailed description of how to make the antibody and provides related sequence information. U.S. Patent No. 5,939,531 further

provides the deposit information about the hybridoma that produced FRP5. The deposit was made under the Budapest Treaty on November 21, 1990 and the patentees assure the availability of such hybridoma. Finally, similar information is set forth in PCT No 95/30014 and European Patent No. 502 812, the later of which is incorporated by reference in the specification at page 5, first paragraph, and which was considered by the PTO on November 29, 2001. Copies of these patents are attached and listed on Form 1449. In any event, the law does not require applicants to put into the specification information that is generally available to the public. In view of the attached publications, which were available to the skilled artisan at the time of filing, applicants urge that the present invention is fully enabled and described.

II. Prior Art Rejections

Claims 2-7, 9-11, 13 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stancovski et al., (Journal of Immunology, 1993, Vol. 11, pp. 6577-6582) in view of Brocker et al. (Eur. J. Immunology, 1993, Vol. 23, pp. 1435-1439, reference AA of the IDS filed 9/22/00) and Horgan et al. (Journal of Immunology, 1993, Vol. 150, pp. 5400-5407). Applicants traverse this rejection and respectfully submit that it was not obvious to generate a hinge-containing, anti-tumor antigen directed, fusion zeta-chain bifunctional protein construct as claimed. The combined teachings of the cited art would not have provided the skilled artisan with an expectation of success.

In fact, Stancovski et al. should be read as teaching against the invention. That is, it teaches that a bifunctional protein without a hinge region might be suitable for killing tumor cells. This teaching is the opposite of what applicants claim. With regard to the elimination of tumor cells by cytotoxic T lymphocytes containing the bifunctional protein as described in the present application, a hinge region is absolutely required for its anti-tumor function. Thus, according to the present invention, a hinge region is absolutely required for its anti-tumor function.

Brocker et al. similarly fail to provide the requisite expectation of success because they do not teach the ability of a hinge region containing construct to work in an experimental setting, targeting tumor cells. This is of particular relevance since tumor cells have usually acquired the ability to withstand killing by the immune system by establishing immune escape mechanisms. Thus, the test system of Brocker et al. would not have been read by the

skilled artisan as demonstrating the functionality of such bifunctional proteins in the fight against tumor cells.

Horgan adds nothing to cure the deficiencies in this art.

Accordingly, applicants respectfully request the Examiner to reconsider and withdraw the rejection under § 103.

Conclusion

In view of the foregoing remarks, reconsideration of the application and allowance of all claims is requested. If there are any issues remaining which the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the local exchange listed

Respectfully submitted,

Date: May 6, 2002

Patricia D. Granados

Patricia D. Granados
Attorney for Applicant
Registration No. 33,683

Customer No. 26633
Heller Ehrman White & McAuliffe, LLP
1666 K Street, N.W., Suite 300
Washington, D.C. 20006
Telephone: (202) 912-2000
Facsimile: (202) 912-2020

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MARKED UP COPY OF AMENDED CLAIMS

2. (First amendment) A DNA encoding a bifunctional protein, wherein said protein comprises [comprising]:

[1)](i) an antigen binding domain derivable from [a monoclonal antibody directed against a suitable antigen on a tumor cell] an anti-ErbB2 antibody;

[2)](ii) a hinge region comprising form about 40 to about 200 amino acids, and

[3)](iii) a functional zeta (ζ) chain derivable from the T-cell antigen receptor (TCR).

3. (First Amendment) A DNA according to claim 2 encoding a protein wherein the antigen binding domain is [a single chain antibody, particularly the single chain antibody designated] FRP5 (scFv(FRP5)).

4. (Second Amendment) A DNA according to claim 2 encoding a protein wherein the hinge region is from an immunoglobulin-like protein [hinge region].